



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2010-D-0589]

Draft Guidance for Industry on Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia: Developing Drugs for Treatment; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia: Developing Drugs for Treatment.” The purpose of this draft guidance is to assist clinical trial sponsors and investigators in the development of antibacterial drugs for the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). The science of clinical trial design and our understanding of this disease have advanced in recent years, and this draft guidance informs sponsors of our current recommendations for clinical development. FDA is specifically requesting comment on critical areas of scientific interest including the appropriate primary efficacy endpoints, the use of an intent-to-treat (ITT) population for the primary analysis population, and the use of antibacterial therapy by patients before participating in clinical trials. This draft guidance revises the draft guidance of the same name that published November 29, 2010.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft

guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Joseph G. Toerner, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6244, Silver Spring, MD 20993-0002, 301-796-1300.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia: Developing Drugs for Treatment.” The purpose of this draft guidance is to assist clinical trial sponsors and investigators in the development of antibacterial drugs for the treatment of HABP/VABP. Issues in HABP/VABP clinical trials were discussed at a 2009 workshop cosponsored by FDA and professional societies. Recently, there have been additional discussions about clinical trial design and endpoints for HABP/VABP at a meeting of the Anti-Infective Drugs Advisory

Committee. As a result of these public discussions, the science of clinical trial design and our understanding of endpoints and approaches to clinical development have advanced.

This draft guidance revises the draft guidance published in November 2010 (75 FR 73107) and informs sponsors of the changes in our recommendations. We acknowledge the challenges in conducting clinical trials of investigational antibacterial drugs in HABP/VABP. This revised draft guidance incorporates changes intended to attain a greater degree of balance between the practicability of conducting HABP/VABP clinical trials and the trial procedures needed for a scientifically sound and interpretable trial. We are requesting input from the public on these changes, for consideration before finalizing the guidance. Specifically, the changes from the 2010 draft guidance include:

- A description of two potential primary efficacy endpoints for HABP/VABP clinical trials: (1) All-cause mortality and (2) all-cause mortality or disease-related complications.
- A justification for a noninferiority margin based on all-cause mortality.
- Suggestions for efficacy analyses based on: (1) An overall ITT population and (2) a microbiological ITT population consisting of those patients who have a documented bacterial pathogen known to cause HABP/VABP.
- Recommendations for enrolling patients who have received prior effective antibacterial drug therapy.

Issuance of this guidance fulfills a portion of the requirements of title VIII, section 804 of the Food and Drug Administration Safety and Innovation Act of 2012 (Pub. L. 112-144), which requires FDA to “review and, as appropriate, revise not fewer than 3 guidance documents per year...for the conduct of clinical trials with respect to antibacterial and antifungal drugs....”

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. The Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulation. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014 and the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001.

III. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: May 1, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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